C4 39. (Once Amended) A composition comprising the protein of claim 36 and an acceptable carrier.

C5 44. (Once Amended) A composition comprising the protein of claim 41 and an acceptable carrier.

C6 49. (Once Amended) A composition comprising the protein of claim 46 and an acceptable carrier.

C7 54. (Once Amended) A composition comprising the protein of claim 51 and an acceptable carrier.

C8 59 (Once Amended) A composition comprising the protein of claim 56 and an acceptable carrier.

C9 64. (Once Amended) A composition comprising the protein of claim 61 and an acceptable carrier.

C10 69. (Once Amended) A composition comprising the protein of claim 66 and an acceptable carrier.

C11 74. ((Once Amended) A composition comprising the protein of claim 71 and an acceptable carrier.

Reply

Double Patenting

The presently pending Office Action indicated that should claims 24, 25, and/or 26 be found allowable, then claims 30, 31, and/or 32, respectively, would be objected to under 37 C.F.R. 1.75 as being substantial duplicates thereof. *See*, Paper No. 13, pages 4-5. In particular, it was asserted that claims 24, 25, and 26 have the same scope as claims 30, 31, and 32, respectively. *Id.* Applicants respectfully disagree with the objection/rejection these claims are substantial duplicates having identical scope.

Applicants respectfully point out that claims 24, 25, and 26 are directed to an isolated protein which comprises amino acids 19-121, 2-121, and 1-121 (respectively) of SEQ ID NO:85. In contrast, claims 30, 31, and 32 are directed to an isolated protein comprising the amino acid sequence of the secreted portion of the polypeptide, the complete polypeptide minus the N-terminal methionine, and the complete polypeptide (respectively) encoded by the HPMBQ91 cDNA contained in ATCC Deposit No. 209070.

Moreover, the M.P.E.P.§ 706.03(k) states:

> Inasmuch as a patent is supposed to be limited to only one invention or, at most, several closely related indivisible inventions, limiting an application to a single claim, or a single claim to each of the related inventions might appear to be logical as well as convenient. However, court decisions have confirmed applicant's right to restate (i.e., by plural claiming) the invention in a reasonable number of ways. Indeed, a mere difference in scope between claims has been held to be enough.

In particular, it is well known by those of ordinary skill in the art that protein signal peptide cleavage does not occur with 100% identical precision in real world biological systems. Indeed, the present specification points out that "in some cases, cleavage of a secreted protein is not entirely uniform, which results in two or more mature species of the protein." *See*, Specification, page 65, lines 20-22. Accordingly, while claim 24 encompasses an isolated protein comprising amino acid residues 19 to 121 of SEQ ID NO:85, the scope of this claim is different from that of claim 30, wherein the secreted portion of the polypeptide encoded by the HPMBQ91 cDNA contained in ATCC

Deposit No. 209070 is expected to be expressed with some naturally occurring variability in signal peptide processing. Hence, the scope of claims 24 and 30 are not identical.

It is also well known by those of ordinary skill in the art that even "complete polypeptides" are not always expressed in real world biological systems with 100% identical precision. For example, it is well-known in the art that ribosomal complexes, translating in tandem on the same mRNA transcript, will very often translate a polypeptide via use of alternate, tandemly positioned start codons. For example, in the present case SEQ ID NO:85 has a methionine residue at position 1 and a second methionine closely thereafter at position 4. Hence, one of ordinary skill in the art would quite readily recognize that within a real world biological expression system the "complete polypeptide" expressed from the HPMBQ91 cDNA contained in ATCC Deposit No. 209070 may sometimes be translated beginning with the methionine residue corresponding to position 1 in SEQ ID NO:85 and sometimes beginning with the methionine residue corresponding to position 4 in SEQ ID NO:85. Both proteins, however, represent the "complete polypeptide" as they are comprised of the entirety of the sequence translated by a real-world ribosomal complex. Hence, the scope of claim 25 compared to claim 31, and the scope of claim 26 compared to claim 32, are not identical.

Accordingly, in view of the above comments, Applicants respectfully submit that in allowing claims 24, 25, and 26, it would be inappropriate to object to claims 30, 31, and 31 as substantial duplicates thereof. Applicants wish to thank the Examiner for the thoughtful consideration of this issue.

Claim Rejections - 35 U.S.C. § 112, First Paragraph [enablement]

Claims 28, 34, 39, 44, 49, 54, 59, 64, 69, and 74 have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly "containing subject matter which was not described in the specification in such a way as to enable one skilled in the art...to make and/or use the invention." *See*, Paper No. 13, pages 5-6. The Office Action recites eight factors which may be considered when determining whether a specification is enabling, or whether undue experimentation would be required to practice the claimed invention. *See*, Paper No. 13, page 6, second paragraph.

In the interest of expediting prosecution of the present application Applicants have herein amended claims 28, 34, 39, 44, 49, 54, 59, 64, 69, and 74. Applicants

respectfully submit that said amendments do not evoke any prosecution history estoppel as to the scope of equivalents to these claims. Applicants do, however, respectfully disagree with the rejection of these claims and submit that the specification is enabling for the invention as claimed, without necessitating undue experimentation.

First, Applicants note the acknowledgement that the present specification teaches that "the instant neurokinin" may modulate smooth muscle or vascularization associated with reproduction, that it is likely that the polypeptides of the instant invention are active in the signal transduction and information processing in the nervous system and, that polypeptides of the instant invention are useful for the diagnosis and treatment of reproductive disorders." *See*, Paper No. 13, page 7 first paragraph. Hence, Applicants respectfully disagree with the allegation that the specification "fails to disclose any pharmaceutical property for the polypeptide of the instant invention." *See*, Paper No. 13, page 8, first full paragraph. In contrast, the present specification identifies the claimed polypeptide as a member of the tachykinin protein family and teaches that, like other tachykinins, this protein may be expected to have pharmaceutical properties such as, for example, the modulation of smooth muscle contraction and vascularization. *See*, Specification, page 35, lines 1-15.

Applicants also respectfully disagree with the rejection premised on an assertion that the specification does not "teach the efficacy of the polypeptide in treating any of the conditions disclosed." *See*, Paper No. 13, page 8, first full paragraph, last sentence. In the first part, considerations of "efficacy" are not listed among the eight factors to be considered under M.P.E.P. § 2164.01(a). Moreover, as explained in the M.P.E.P., considerations of "efficacy" fall under jurisdiction of the U.S. Food and Drug Administration, not the U.S.P.T.O. *See*, M.P.E.P., § 2164.05, third paragraph ("Testing for full safety and effectiveness of a prosthetic device is more properly left to the [FDA]."). Further, the M.P.E.P. § 2107.03 instructs that it is "...improper for Office personnel to request evidence of safety in the treatment of humans, or regarding the degree of effectiveness."

Applicants also respectfully submit that rejection expressed under "Skill level of the artisan, Predictability of the invention and amount of experimentation necessary" is premised on an inaccurate characterization of the teachings in Patak et al. *Clin. Exp. Pharmacol. Physiol.*, 27:922-927 (2000). *See*, Paper No. 13, page 8 last paragraph. In particular, it was asserted that "Patak et. al...teach that of the three

studied tachykinins (substance P, neurokinin A and neurokinin B), only NKA elicited uterine contraction response in tissue from pregnant women (page 924, left column, first paragraph)." Applicants, however, were unable to find any such statement in Patak et al., page 924, left column. Moreover, the assertion is contradictory to the teachings of Patak et al For example, Patak et al. teaches that neurokinin B is approximately equal to Substance P in its ability to cause uterine contractions in rats. *See*, Patak et al., page 924, right column, third paragraph ("In this species, the relative order of potency of the tachykinins in causing contraction of the uterus of oestrogen-primed and untreated non-pregnant rats is NKA > SP ≈ NKB.") Furthermore, although Patak et al. characterize NKA as more potent than NKB in causing uterine contractions in women, these investigators have, in fact, found NKB to cause uterine contractions. *See*, Patak et al., page 925, left column, first paragraph ("[R]ecent studies in our laboratories clearly indicate that, in the presence of peptidase inhibitors, the mammalian tachykinins SP, NKA and NKB elicit reproducible, concentration-dependent contraction of uterine tissue obtained from both pregnant and non-pregnant women...").

In sum, although Applicants have herein amended claims 28, 34, 39, 44, 49, 54, 59, 64, 69, and 74 solely to expedite prosecution of the present application, Applicants reserve the right to pursue the subject matter encompassed by the unamended claims in one or more subsequent divisional or continuation applications.

Claim Rejections - 35 U.S.C. § 112, First Paragraph [possession]

Claims 27, 33, 36-75 have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly "containing subject matter which was not described in the specification in such a way as to reasonably convey...that the inventor(s), at the time the application was filed, had possession of the claimed invention." See, Paper No. 13, page 11, first paragraph. These claims are directed to heterologous polypeptides, 90% and 95% identical polypeptides, and polypeptides comprising 30 and 50 contiguous amino acids.

The present rejection particularly alleges that "[t]he specification does not 'clearly allow persons of ordinary skill in the art to recognize that [he or she] invented

what is claimed.' Vas-Cath Inc. v. Mahurkar 19UGPQ2d at 1116." *See*, Paper No. 13, page 11, third paragraph. Applicants respectfully submit that this conclusion tremendously underestimates the ability of those of ordinary skill in the relevant art. Indeed, given the polypeptide sequence of SEQ ID NO:85 or the polypeptide encoded by the HPMBQ91 cDNA contained in ATCC Deposit No. 209070, one of ordinary skill in the art would quite readily recognize Applicants had possession of the claimed invention. An assertion to the contrary, is an assertion that one of ordinary skill *would not be able* to recognize polypeptide sequences comprised within the amino acid sequence shown in SEQ ID NO:85 or encoded by the HPMBQ91 cDNA; including polypeptides 90% or 95% identical thereto, or said polypeptides with additional heterologous sequences. Applicants submit that such an assertion greatly misrepresents the ability of those of ordinary skill in the art.

The present Office Action acknowledges that possession may be shown "by describing the invention with sufficient relevant identifying characteristics (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention." See, Paper No. 13, page 12, first paragraph. Applicants point out that the present specification does, in fact, demonstrate possession by providing adequate description of the invention with sufficient relevant identifying characteristics. The present specification provides both a specific polypeptide sequence (i.e. SEQ ID NO:85) and also an ATCC Deposit which demonstrate possession of the claimed invention. Likewise, the specification describes specific mathematical formulae (90% and 95% identity; 30 and 50 contiguous amino acids) which may be used to identify the claimed invention.

The present Office Action asserts that:

> The skilled artisan cannot envision the detailed chemical structure of the encompassed sequences isolated from other species, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it.

See, Paper No. 13, page 12, first paragraph.

Applicants respectfully disagree with the above assertion and point out that the presently pending claims are not directed to "sequences isolated from other species."

Instead, as discussed above, the claimed polypeptides have be claimed by providing both an explicit amino acid sequence and also a biological deposit. And, embodiments of the invention have been described and claimed according to precise, quantifiable mathematical formulae. Hence, the present specification and pending claims provide much more than "a mere statement that it is part of the invention."

The present Office Action also alleges that "since structure and/or function cannot be predicted from [the] sequence, no identifying characteristics are provided for the claimed genus of sequences ..Thus, it is concluded that the written description requirement is not satisfied for the claimed sequences and polypeptides." *See*, Paper No. 13, page 13, first paragraph. Applicants respectfully disagree. As discussed above, the structure of the claimed polypeptides and identifying characteristics have been provided for the claim genus of sequences via provision of an explicit amino acid sequence, a biological deposit, and, provision of precise, quantifiable mathematical formulae with which to predict and identify all members of the claimed genus.

Furthermore, Applicants respectfully submit that the legal reasoning used, as quoted above, is clearly improper even by the written description guidelines. The rejection that "a conception is not achieved until reduction to practice has occurred" is neither supported by the U.S.P.T.O. Guidelines nor by case law. As stated in the Revised Written description Guidelines (Fed. Reg. Vol 66, No. 4, Section I, page 1104, Friday, January 5, 2001, emphasis added):

> To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. Possession may be shown *in a variety of ways* including description of an actual reduction to practice, *or* by showing that the invention was "ready for patenting" such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, *or* by describing *distinguishing characteristics* sufficient to show that the applicant was in possession of the claimed invention

Therefore, *requiring* a reduction to practice to show conception as the *only* way to satisfy written description is incorrect by the U.S. Patent Office's own guidelines. Such a requirement also flies in the face of the underlying principles of

filing a patent application; it in effect nullifies the practice of a constructive reduction to practice (*e g.*, filing a patent application) and placing the public on early notice of the subject matter in the application. This cannot be the purpose of the Written Description Guidelines.

Accordingly, Applicants respectfully submit that the specification conveys with reasonable clarity that Applicants were in possession of the claimed invention. Accordingly, Applicants respectfully request that the rejection of the claims under 35 U.S.C. § 112, first paragraph for inadequate description, be reconsidered and withdrawn.

Claim Rejections - 35 U.S.C. § 112, Second Paragraph

Claims 24-27, 29-35, 38, 41-44, 48, 53, 58, 63, 68, and 73 were rejected under 35 U.S.C. § 112, second paragraph, as allegedly "being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." *See*, Paper No. 13, page 13.

In particular, claim 24 was alleged to be indefinite in its recitation of "comprising amino acid residues 19 to 121 of SEQ ID NO:85" *Id.* And, claims 25-29 were rejected insofar as they depend from claim 24. *See*, Paper No. 13, pages 13-14. Applicants have herein amended claim 24 in accordance with the Examiner's suggestion. Applicants assert that this claim amendment is merely cosmetic and is no way intended, nor should it be construed, to further limit the scope of the claim subject matter. In view of the amendment to claim 24, Applicants respectfully request that the rejection of claims 24-29 be withdrawn.

Claims 25 and 26 were rejected for allegedly being indefinite because "they fail to further limit the subject matter of claim 24 from which they depend." *See*, Paper No. 13, page 14, first full paragraph. Applicants respectfully disagree and point out that claim 24 is, in fact, broader in scope than claim 25, which is, likewise, broader in scope than claim 26. Applicants point out that because claims 24-26 use comprising language, shorter polypeptide sequences actually encompass a broader scope than longer polypeptide sequences. This is because claim 24, for example, requires fewer amino acids of SEQ ID NO:2 than do the subsequent dependent claims. Claims 31 and 32 were also rejected on the same grounds. *See*, Paper No. 13, page 14-15. Applicants point out that the same analysis applies to claims 31 and 32.

Accordingly, Applicants submit that this rejection of claims 25, 26, 31, and 32 is improper and respectfully request that it be withdrawn. Should the Examiner remain uncertain of Applicants' discussion above, the Examiner is welcome to contact the undersigned for any clarification.

Claims 30 and 41 were rejected as being indefinite "in their recitation of 'secreted portion of the polypeptide encoded by the HPMBQ91 cDNA contained in ATCC Deposit No. 209070" as compared to the disclosure in Table 1 on page 58 of the specification. *See*, Paper No. 13, page 14. Clarification or correction was requested. *Id.* Accordingly, Applicants would like to clarify that there is not a discrepancy between the predicted secreted portions of the polypeptides shown for SEQ ID NO:68 and SEQ ID NO:85 in Table 1 and the polypeptides encompassed by claims 30 and 41. First, as discussed above, signal sequence cleavage is not a 100% identically precise process in real world biological systems, nor can signal peptide cleavage be predicted with 100% certainty (as discussed in the present specification at pages 65 through 66). Hence, the predicted signal peptides for SEQ ID NO:s 68 and 85 as presented in Table 1 reflect equally likely predictions on where signal peptide cleavage may be expected to occur in the corresponding polypeptide sequences. Second, also as discussed above, the secreted portion of the polypeptide encoded by the HPMBQ91 cDNA contained in ATCC Deposit No. 209070 is not constrained by the predictions set forth in Table 1, instead the secreted portion of the polypeptide encoded by the HPMBQ91 cDNA is governed by the real world biological system in which it is expressed. Accordingly, in view of this clarification, Applicants respectfully request that the rejection of claims 30 and 41 (as well as 31-35 and 42-44 insofar as they depend from claims 30 and 41, respectively) be withdrawn.

Claims 27, 33, 38, 43, 48, 53, 58, 63, 68, and 73 were rejected as allegedly being indefinite "in their recitation of 'a polypeptide sequence heterologous to SEQ ID NO:85.'" *See*, Paper No. 13, page 15. In particular, it was asserted that "[t]he context in which the term [heterologous] is used in the instant claims and how two sequences can be heterologous to each other is not clear." And that, "[t]he term 'heterologous' is usually used to refer to a gene or protein which is being expressed in an organism or cell in which it is not normally present." *Id.* In this regard, Applicants point out that the present specification defines, describes, and provides examples of heterologous polypeptide sequences as "polypeptides of different proteins" (i.e. polypeptide sequences not naturally conjoined). For example, see the specification at